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EDITORIAL

THE EXTENSION OF PHARMACOPŒIAL USEFULNESS

THE unremitting activities of the present Chairman of the United States Pharmacopœia Revision Committee and its forward-looking Board of Trustees are bearing fruit in a brand new adventure for that august institution. Not content with having given the health professions a pharmacopœia that can well claim leadership among the world's standard books of medicine, an extension program is now actively under way to familiarize the professions, as they have never before been familiarized, with every aspect of Pharmacopœia usefulness.

They propose to make of the Pharmacopœia a real instrument, and not a mere ornament, and their plans for this accomplishment are comprehensive and already under way. The physician, from interne to private practitioner, and every pharmacist in the country may profitably participate in the program of education and the ultimate results are bound to be of benefit to both professions and, of course, to public health.

From a communication recently received from the Committee we quote the following informative paragraphs. Those desiring additional information pertaining to these plans should get into touch with Dr. E. Fullerton Cook, Philadelphia, the Chairman of the U. S. P. Revision Committee.

"The therapeutically useful substances recognized by the Pharmacopœia have been intended, in each revision, to represent the most widely used medicines of that generation and decisions as to 'admissions' and 'deletions' early, in each Revision, become one of the most important responsibilities of the Revision Committee.

During the last three revisions this feature has been particularly important since the medical profession, during that period, has revolutionized the methods for evaluating therapeutic efficience and has been demanding satisfactory evidence of clinical value before accepting a new medicinal product.

In the current Revision this feature of the program has been especially emphasized and the Sub-Committee on Scope has earnestly endeavored to establish a list of official medicines which could be depended upon to represent the most advanced knowledge of therapeutics. The Scope Sub-Committee has been equally determined that these be limited to dependable medicines and also that they cover every need of the physician, so far as such products were available.

With the publication of the Eleventh Revision, the Committee has authorized a program which subjects these decisions on scope to a most searching review, and at the same time provides for its prompt revision should that seem wise in the light of new information.

To carry out this program and at the same time widely extend authentic information to physicians concerning the use of official medicines, a special Committee was appointed which is now carrying out an intensive program through the wholehearted cooperation of the American Medical Association. Every feature of this program has received the approval of both the U. S. P. and the A. M. A. representatives before adoption.

It was decided that a series of articles presenting the therapeutic side of specific diseases, or dealing with substances having similar physiologic activity would be published in the *Journal of the American Medical Association,* one article to appear each two weeks for at least a year. When the first twenty-four titles had been selected after the study of fifty or more which had been proposed, the eighteen physician members of the U. S. P. Committee were invited to suggest the names of clinicians especially well qualified to prepare the articles. A half dozen or more names were suggested for each subject and from these one physician was selected, by mutual agreement, to be invited to write the article. (These articles are now appearing in the *Journal of the American Medical Association.*)

Already eighteen of these completed papers have been received and submitted for review and approval to both the U. S. P. and the A. M. A. groups. Each article is to be about 3000 words in length, corresponding to about five columns in the *A. M. A. Journal.*

It was further realized that unless some plan could be developed for more specifically calling the attention of physicians to these presentations than would result from their initial publication in the *Journal,* that they would largely fail to perform their purpose. Therefore certain additional features have been developed as outlined below:

An auxiliary Committee of professional pharmacists was appointed to assist in preparing a corresponding series of articles to go to the pharmaceutical press and also to plan a series of exhibits which would graphically call attention to each article. These exhibits are to be set up first in the headquarters of the Philadelphia County Medical Society at the same time that the medical article appears in the *A. M. A. Journal* and an illustration and description of these exhibits will be made a feature of each pharmaceutical article. These parallel pharmaceutical articles, calling attention to the medical article appearing on a specific date in the *A. M. A. Journal,* will be set up in advance by the *A. Ph. A. Journal,* reprints will be made, carrying a release date, which date will be the same as that of the medical article, and all journals, which care to do so, can publish the articles simultaneously. It will be sent to seventy or more pharmaceutical journals and it is hoped that many will regularly publish it under the caption of 'The Pharmacopœia' for the information and guidance of pharmacists throughout the country.

It is planned that reprints of the medical article will also be made available, through the office of the Chairman of the U. S. P. Committee of Revision, so that pharmacists can get these promply to present regularly to their physician friends. These reprints will be punched and an attractive cover provided, so that by the end of the year the physician receiving the reprints from his pharmacist friend, each two weeks, will have a valuable text on therapeutics which he is likely to consider worth keeping and using. It is expected that each article will suggest a number of prescriptions and the pharmacist, in presenting the reprint to a physician can also leave with him one of the prescriptions suggested, filled in his own pharmacy, and illustrative of the professional qualifications of the pharmacist.

A feature of the plan also includes the ultimate publication of the series as a bound book, to be thus made available to students in medical schools, to medical internes, and to physicians in practice.

It is also hoped that exhibits, covering each article, will be made in many hospitals throughout the country, also at the headquarters of many County Medical Societies, and before state and national medical conventions."

It is to be hoped that all who are genuinely interested in the promotion of the profession of pharmacy will recognize in this movement, an opportunity, and a responsibility for the performance of a really creditable service to the professions and to humanity.

IVOR GRIFFITH.

ORIGINAL ARTICLES

BUILDING CASTLES OF HEALTH

By Louis Gershenfeld, Ph. M., B. Sc., P. D.

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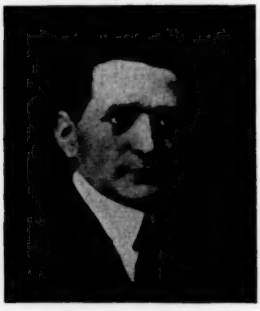
ENGINEERS are building vast structures for the future so as to benefit mankind. But what is being done so that humans may be enabled to enjoy these accomplishments and that they may find life and living desirable and happier? Disease prevention is the answer. It is true that progress has been made in preventive medicine, but if we are to accomplish worthwhile results on a large scale, it is high time the fact is recognized that more co-operation by everyone is needed. Each and every one has a part and must do their share in the building of Castles of Health. Unfortunately, there is a deplorable ignorance in regard to what co-operation and efficient service really imply. Let us therefore consider two scourges, smallpox and diphtheria, which for hundreds of years have been reducing life and causing untold suffering. These dreaded scourges can be eradicated and we can be protected from such disasters if the effort of co-operation is vigorous enough and the resources are adequate for the job on hand.



Louis Gershenfeld, Ph. M., B. Sc., P. D.

SMALLPOX—AN ANCIENT DISEASE

Smallpox has been a scourge of mankind attacking all ages and all races, prevailing in all countries over the entire globe and occurring throughout all periods of man's existence. During the Byzantine Period (476-732 A. D.), we find many descriptions of earlier epidemics of smallpox presented by Fathers of the Christian Church. Eusebius described a Syrian epidemic in 302 A. D. Gregory of Tours described one in 581 and Marius, Bishop of Avenches was the first to employ the term "variola" in 570. The Irish monastery records of 675 A. D. speak of smallpox as "Bolgagh" and "Galar Breac." Aaron, a prominent seventh century chronicler, describes smallpox (as cited in the "Continent" of Rhazes). The oldest Japanese medical

book, the Ishinho, written by Yasuhori Tambu in 982 records the existence of isolation houses for smallpox patients. Rhazes (860-932), the great Persian clinician and the greatest physician of the Eastern or Bagdad Caliphate gives an account of smallpox which is so vivid and complete that it is almost modern. His description of this dreaded affection, a classic text, is the first authentic account in literature. In this treatise, he mentions that Galen was familiar with smallpox and he quotes Aaron of Alexandria, the Arabian-Jewish physician Masarjawaih and his teacher the distinguished Ali al-Tabari who became a Mohammedan but was the son of Sahl, a well-known Jewish scholar and scientist. Haly ben Abbas (died in 994), another well-known Persian medical practitioner, was the author of Almaleki ("Liber regius" or "Royal Book"), a work which was the canonical treatise on medicine for almost a century. It was never printed in the original Arabic but was translated into Latin in 1080 by Constantinus Africanus who published it as his own work. This translation contains a description of smallpox and also the Latin term for the latter (variola). Rhazes' encyclopedic "Continent of Medicine" was superseded by Abbas' "Royal Book" and the latter was later supplanted by Avicenna's twenty-volume treatise, the Cannon. It was Avicenna, the Ibn Sina of the Arabians, who was the first one to speak of smallpox and measles as "of all diseases the most contagious". Avenzoar (1113-62), sage of Seville, descendant from a family of physicians made the interesting and original observation that smallpox does not attack the same person twice. One of the early English physicians, Gilbertus Anglicus (died in 1250), who was the leading exponent of Anglo-Norman medicine, also refers to smallpox as a contagious disease, a view which was even afterward contradicted by the distinguished Thomas Sydenham (1624-89).

THE ANNUAL TOLL

In the 15th and 16th centuries, epidemics of smallpox appeared in Europe in the northern countries, in particular in Germany (1493) and in Sweden (1578). In the 17th century, this disease raged throughout the European continent during 1614 and in England again from 1666 to 1675. During the latter part of the 17th century, an annual average of over one thousand deaths due to smallpox occurred in London. There evidently must have prevailed at least five thousand cases annually in this city alone, if we figure that one in each five cases is fatal. Official figures are available revealing where town after

town in Europe was visited by this scourge and but few of the population remained who had not been attacked by smallpox. Writers during the 18th century estimated that an average of 600,000 human beings throughout the world died annually of smallpox. Europe alone claimed over 200,000 victims each year. During the 18th century alone, sixty million humans were lost. Smallpox was introduced into the western hemisphere by the Spaniards about fifteen years after the discovery of America. In Mexico and South America, epidemics of smallpox among the Indians wiped entire tribes out of existence. Six millions of the twelve millions of American Indians fell victims of smallpox. In the year 1633-34, smallpox swept away large numbers of both colonists and Indians in New England and thirty years later (1664), a most devastating epidemic of this scourge spread throughout the Dutch colony of New Netherlands. Similar epidemics appear again in New England during 1666, 1677-78, 1689-90, 1692-93, in 1702 and later during the 18th century. We hear of the frequent proclamations of fasts which were held to avert the ravages of smallpox and subsequently the holding of days of thanksgiving when the epidemic ceased to take its death toll. The only medical publication of the New England colonists in the 17th century was the "Brief Rule to Guide the Common People of New England How to Order Themselves and Theirs in the Small Pocks or Measles," (Boston, 1677) written by Thomas Thacher (1620-78), clergyman and medical practitioner. Many outbreaks occurred throughout New England during this and the following century, reaching Pennsylvania in 1661 and Charleston, S. C., in 1699. In Iceland, in 1707, according to records of the government of Denmark, 18,000 died out of a population of 50,000 or 36 per cent. of the inhabitants were wiped out by smallpox within one year. In 1734, in the Danish settlement in Greenland, two-thirds of the inhabitants were killed by a devastating epidemic of smallpox. In the epidemic of 1752 which raged in Boston, by the time the malady was over, excluding the 1845 persons who left the town to avoid contracting the disease, only 174 remained out of a population of 15,684 who never had smallpox.

COLONIAL SMALLPOX

The ship which brought William Penn to this country in 1682 lost thirty of its passengers on the voyage due to an epidemic of smallpox. In Philadelphia, smallpox epidemics were common and much discussion prevailed concerning methods of handling the cases of this disease. During

the latter part of the 18th century, many serious outbreaks occurred among the inhabitants of the City of Brotherly Love and in other communities found among the colonies. It is of interest to note that many laws were enacted even at a very early period, bearing upon the prevention and contraction, the spread, the reporting and the isolation, etc., of smallpox. This brings us to the period of Edward Jenner of England (1749-1823), the son of a Gloucestershire clergyman, who presented one of the greatest triumphs in the history of medicine.

Now allow me to direct your attention to some important facts concerning this serious disease. Smallpox, a highly contagious affection, is one of the most fatal of the acute diseases. It is difficult for us to appreciate that at one time it was more common than measles, and during the 18th century, of which the best records are available, almost everyone had the disease before adult age and usually before the seventh year of life was reached. It is estimated as mentioned previously that more than one-half million died annually. In fact it is claimed that in the 18th century every tenth death was due to smallpox. None escaped. Mothers only counted their children after they had passed through smallpox. Everyone seemed to feel that it was natural and even necessary to pass through an attack of this disease at some period of one's life. The Germans had a proverb: "From love and smallpox but few remain free". It attacked and attacks rich and poor, high and low, the clean and the dirty, all sexes, ages and races, in fact anyone and everyone, anywhere and everywhere. Kings, queens and royalty were among its victims. Smallpox crippled William the Third of England and killed his wife, the Queen. Lord Macaulay, writing of "the most terrible of all of the ministers of death" and describing the untimely death from smallpox in 1694 of the beautiful and young Queen Mary, gives a vivid picture of the ravages of this scourge. Louis XV of France and many others were not spared. The first president of these United States contracted smallpox while in the West Indies. Smallpox or variola is an acute contagious disease characterized by pronounced chills, sudden fever, aches, nausea and vomiting and an eruption. The latter after passing through various stages of papule, vesicle and pustule, dries up, and distinct scars remain. When the pocks are separated from each other by areas of skin free of eruption, the disease is known as discrete or distinct smallpox in contrast to a more severe form,

confluent smallpox, the name employed when the vesicles and pustules run together, usually covering extensive areas of the skin surface.

THE BLACK SMALLPOX

The most fatal type of smallpox is that known as hemorrhagic or "black smallpox". In the latter type before the characteristic eruption can develop, blood-spots appear due to the occurrence of hemorrhages into the skin and mucous membranes and death results usually within a few days. Smallpox was a frequent cause of blindness in days gone by and one-eighth of all the blindness in Europe before vaccination became general was due to smallpox. Apparently no one or very few possess a natural resistance (a natural immunity). Smallpox, at one time the most prevalent and then as now a dreaded scourge, is a loathsome disease, for those who recover are most frequently mutilated and disfigured, maimed or deformed and even blinded for life. The unsightly permanent pitting or scarring of the face is almost always present except in the very mild cases. Pauper-woman and royal-lady were speckled with pock-holes. It granted nor grants favors to anyone. The nature of the agent which causes smallpox is still unknown and is spoken of as a virus. Whatever the actual causative agent may be, it is certain that this disease is transmitted with extreme ease, actual contact, direct or indirect with a smallpox patient being unnecessary for its transmission. The diseases smallpox, cowpox, horsepox, and sheeppox, if not identical are closely allied. The first two, smallpox or variola and cowpox or vaccinia, if not one and the same condition are at least very closely related. While we do not know definitely how the virus of smallpox enters the human system, many considerations have made it seem plausible that entrance into the body is through the mucous membranes of the upper respiratory tract.

PROTECTION AGAINST SMALLPOX

Our knowledge concerning protection against this malady is fortunately more advanced than is that of the cause. Though there is no specific remedy available in the treatment of smallpox, there is in use today a sure and complete safeguard against this scourge. It has been known for centuries that one attack of smallpox, usually protects against subsequent attacks (though not necessarily in all cases). This knowledge was made use of in what became known as "variolation" or "inoculation" or exposing young healthy children to infection during mild outbreaks, hoping that mild attacks would result which would confer a lasting resistance or immunity.

INOCULATION OR VARIOLATION

This old custom of inoculation was practiced by the Chinese from time immemorial. The physicians in ancient India and other countries appear to have knowledge of this fact. In more recent days we find that in 1717, the Royal Society in London received a communication from a Doctor Woodward who described the practice of inoculation among the Turks; and a Doctor Timoni (in 1714), a Mr. Kennedy (in 1715) and Doctor Pylarini (in 1715) related other accounts of this Turkish method. In April, 1721, Lady Mary Wortley Montagu, returning to England from Turkey introduced to the English more generally the practice of inoculation for smallpox after her own son had been "engrafted" with a successful outcome. This practice became popular on the Continent and spread to America when the Rev. Dr. Cotton Mather of Boston suggested its use to combat the ravages of smallpox. It is interesting to note that most of the medical men in Boston ridiculed the Reverend Mather's suggestion and in fact scorned the entire proposition. It was only his warm personal friend Dr. Zabdiel Boylston, eminent as a medical practitioner, botanist and zoologist who recognized the value of this method of protection and set out to employ this technique so as to stamp out smallpox. Only two months after the inoculation method was introduced into England, Dr. Boylston began its practice in this country when on June 27, 1721, he inoculated his only son (a boy of thirteen) and two negro servants. The results were completely successful and during the latter part of 1721 and the early part of 1722, Dr. Boylston inoculated 247 persons and 39 were inoculated by other persons in Boston and its vicinity. Of this number only six, or 2 per cent. of the total, died and several of the latter are said to have either taken the infection before inoculation or died from other affections. During the same period there were 5759 cases of smallpox contracted naturally in Boston; and of the latter, 844 or almost 15 per cent. died, and many of those who recovered were maimed or disfigured for life. But many medical practitioners and laymen, especially clergymen, denounced Mathers and Boylston and the practice of inoculation. The opponents of these two well-meaning gentlemen stopped at nothing in their denunciatory utterances and in the malicious methods they employed against them, and though Dr. Boylston's character for a long period was besmirched, his efforts to aid mankind were rewarded later. The practice of inoculation for smallpox was apparently confined

solely to Boston and its immediate vicinity until the epidemic of 1730 in Philadelphia, when J. Growden, Esq., a well-known citizen, was the first person in the latter city to have been successfully treated. In the epidemics of 1736-37 in Philadelphia, 129 patients were inoculated and of this number only one, an infant, died. But opposition to the method prevailed, though it is of interest to note that Benjamin Franklin was one of the staunchest advocators of inoculation. In his "Autobiography" he mentions the loss in 1736 of a son who died after having contracted smallpox. He says: "A fine boy of four years old, by the smallpox, taken in the common way. I long regretted him, and still regret that I had not given it to him by inoculation. This I mention for the sake of parents who omit that operation, on the supposition that they should never forgive themselves if a child died under it, my example showing that the regret may be the same either way, and therefore that the safer should be chosen."

The opposition to inoculation was at times very vehement and proclamations were even issued against its practice. But as each succeeding outbreak of smallpox served to demonstrate that those who were previously inoculated were immune and had not contracted the dreaded disease during the existing epidemic, the practice of this method of immunization (creating a resistance) progressively gained ground in spite of even bitter opposition.

The method of inoculation (known at times as variola inoculata or inoculated smallpox) which was practiced and is said to be still in existence in some Central African countries even at this late date is practically identical with that of vaccination as used today. The difference between the two techniques lies in the material employed in the technique of immunization. In the inoculation procedure, the matter is obtained from the vesicle or pustule of a case of active smallpox but the mild disease which usually develops is however just as communicable as true smallpox; and those who may contract the infection in this way develop true smallpox which may reveal itself in a serious form and prove fatal.

THE MENACE OF INOCULATION

INOCULATION RESULTS IN CREATING AN IMMUNITY IN THE INDIVIDUAL THUS PROTECTING HIM BUT IT MAY ENDANGER THE COMMUNITY AT LARGE.

During inoculation (NOT VACCINATION) there was and is always the danger that the virus may spread to others without notice. When this occurs, the severity of each case increases so that

the disease may then be very easily caught, become widespread, and smallpox may prevail in epidemic proportions. In order to avoid the latter, it became customary for practitioners of inoculation to fit up private houses as hospitals in which their patients could be kept or isolated during the period of passage through the mild attack of smallpox caused by the inoculating procedure. "Taking smallpox by way of inoculation" became a specialty and inoculating hospitals were opened in isolated districts near many communities. During the epidemic of 1773 in Philadelphia, a Doctor Glentworth opened an inoculation hospital in our city; and in the epidemic of 1774, eight prominent medical practitioners volunteered their services to a "Society for Inoculating the Poor." It is of interest to note that the inoculation method as practiced to create immunity against smallpox is the most interesting chapter in the development of modern preventive medicine in that this procedure was animal experimentation on a large scale, but instead of lower animals man himself served as the subject.

VACCINATION While dangerous in the extreme, "variolation" or "inoculation" nevertheless was not without a considerable amount of benefit. But this practice as a universal and lasting method of choice to produce an immunity against smallpox was made unnecessary by the classical work of Edward Jenner of England published in 1798. It was through the controlled observations and carefully planned experiments of this worker that a practice in vogue (inoculation) was converted into an important scientific principle and the basis of modern prophylaxis. Jenner also placed a popular belief upon a scientific plane. As a medical student, he heard a young girl who sought his medical advice say: "I cannot take smallpox because I have had cowpox." This remark made a deep impression upon him and during an investigation he found that country people who had been infected with cowpox were usually immune against smallpox. Cowpox or vaccinia (coming from the Latin, vacca, meaning cow) is an acute mild disease to which many animals including rabbits, cattle, man, monkeys, etc., are susceptible; and when uncomplicated it has never been known to cause death or leave any outward effect. The causative agent of this condition is spoken of as vaccine virus and is to be found in the material present in the skin eruption of those animals having vaccinia or cowpox. Jenner's original observations and experimentation on May 14, 1796,

consisted in transferring the vaccine virus from the material in an eruption (pus from a cowpox lesion) on the hand of a dairy maid (Sarah Nelms) to the arm of James Phipps (eight years of age). Two months later, the same boy was inoculated with material from a smallpox postule without having contracted any subsequent disease or ill effects. Jenner then inoculated smallpox matter into ten other persons who had at some time previously contracted cowpox and no ill effects were apparent. In all fairness to this careful and able worker let it be said that Jenner who himself had been inoculated (not vaccinated) when a boy had been employing in the latter experiment a technique (using smallpox matter) which was in fact an acknowledged method of developing immunity against smallpox (as previously mentioned).

JEFFERSON TO JENNER

Jenner proved by the above experiments that cowpox, a very mild disease in man, is readily transferred and that an attack of this disease and the immunity created protect against smallpox. It was in 1798 that Jenner published his "Inquiry into the Causes and Effects of the Variolae Vaccinae." May I direct your attention to the statement contained in a letter which Thomas Jefferson wrote in 1806 to Jenner: "Future nations will know by history only that the loathsome smallpox has existed and by you has been extirpated." How well this prophecy has been fulfilled is for you to judge. The term vaccination then possessing a specific meaning came into use and referred to the method of transferring the virus from the skin eruption of an animal having vaccinia or cowpox into the skin of another animal. Such vaccine virus is obtained today from calves, but may also be obtained from older cattle, goats, horses, mules, rabbits and other mammals.

Dr. Benjamin Waterhouse, professor of medicine at Harvard, was the first to introduce the practice of vaccination into this country when in July, 1800, he vaccinated his own son with some vaccine virus obtained from England. He then vaccinated his other three children, afterward exposing them to active cases of smallpox without any of them contracting the latter. Dr. James Jackson (1777-1867) later to become professor of Clinical Medicine at Harvard, returned to Boston during the latter part of 1800 after studying under Dr. Woodville of the St. Pancras Smallpox and Inoculation Hospital in London, England, who next to Jenner was the most noted authority on vaccination. Jackson brought back with him a supply of

"cowpox matter" and published an announcement in the *Columbian Sentinel* that he was prepared to vaccinate with it. A Dr. Crawford of Baltimore procured some virus from London and successfully vaccinated several people. Others followed suit. In Philadelphia, Dr. John Redman Coxe (1773-1864), professor of materia medica and pharmacy at the University of Pennsylvania, procured some virus directly from Jenner and performed the first vaccination in that city upon his infant son. He then exposed him to contagion to prove the efficacy of the procedure. The *Columbian Sentinel* of December 18, 1802, contains a report signed by eleven physicians who attest to a most interesting series of experiments which were conducted under the auspices of the Board of Health of Boston. The latter equipped a hospital on Noddle's Island on August 16, 1802, and nineteen boys were vaccinated. On November 9, twelve of the latter and also a son of a Doctor Bartlett, who previously contracted cowpox, were inoculated with material taken from a smallpox patient. No ill effects were apparent in these cases, though the typical reaction was produced when inoculation was made on two individuals who were not vaccinated and who had not been stricken with cowpox. An attempt to again infect the nineteen boys with the material from the two control cases also was unsuccessful. On May 26, 1809, the following advertisement appeared in the Missouri Gazette: "Dr. Saugrain gives notice of the first vaccine matter brought to St. Louis. Indigent persons, paupers and Indians vaccinated gratuitously." In "Colonel Landman's Travels," this army officer, who was stationed at Quebec, relates that he received from England during the winter of 1801-02 vaccine lymph which he tried on the children of a friend named Blackwell, the first case in British North America. In the early spring of 1802, Dr. Joseph Norman Bond, of Yarmouth, N. S., received from his brother in Bath, England, an intimate friend of Jenner, a small quantity of vaccine lymph. He employed it on his own child, an infant of only a few weeks, and then tested its efficacy by inoculating the child with smallpox. This child later, as a medical practitioner, was constantly exposed to smallpox but never contracted the disease.

The first community in this country to offer free vaccination was the town of Milton in the State of Massachusetts; and in 1809, 377 were vaccinated, twelve of whom were found immune to smallpox when inoculated by Dr. Amos Holbrook. These facts are found

in a pamphlet published by the town. Bedford, Massachusetts, offered free vaccination to its residents about the same time and on March 10, 1810, we find an act was passed by the General Court of Massachusetts directing the towns in the state to appoint committees to superintend the vaccination of their citizens and for the towns themselves to bear the expense.

COMPULSORY VACCINATION

So firmly fixed in the minds of those living today in large communities in this country is the notion that compulsory vaccination against smallpox is and must be a distinct part of American life that it may come as a shock to many to realize that there is no national law on the subject of vaccination and that compulsory general vaccination in this country can be said to exist by law only in Kentucky, the Philippine Islands and Puerto Rico. In Massachusetts and Alabama such an obligatory law prevails but is of a local optional character. Maryland, New Mexico, and Hawaii have laws requiring vaccination of children during infancy. Many states have regulations for general compulsory vaccination only when this is deemed necessary for the public health or safety by a local board of health. Most states or first and second-class cities have laws requiring vaccination before admission to the public schools but in many instances this does not affect children living in villages or adults not attending school. There are a few states (Arizona, Minnesota, North Dakota and Utah) which have statutory provisions against compulsory vaccination, the first two named states requiring however that during epidemics of smallpox, unvaccinated children may be excluded from attending school. A provision of the South Dakota statutes makes it unlawful to employ physical force to submit to vaccination. The laws regulating vaccination were held valid by decisions of state supreme tribunals and the U. S. Supreme Court. In our own city, public vaccination was performed indifferently until 1860 when its performance was transferred to the Philadelphia Board of Health. The Act of Assembly of 1895 prohibiting the attendance at school of all unvaccinated children has had a salutary effect. A child who has had smallpox is admitted without vaccination. This regulation makes vaccination compulsory for school children only.

The late Drs. Wm. M. Welch and Jay F. Schamberg reported on approximately 10,000 cases of smallpox treated in the Municipal Hospital in our city between 1870 and 1904. Their observations on

the mortality of the incidence of this disease in vaccinated and unvaccinated persons are of interest:

	Cases	Deaths	Per Cent. of Deaths
Vaccinated in Infancy—good scars....	2,718	167	6.16
Vaccinated in Infancy—fair scars....	1,238	146	11.79
Vaccinated in Infancy—poor scars.. ..	1,673	364	21.75
Total vaccinated scars.....	5,629	677	12.02
Unvaccinated	4,348	1,826	42.00
Total	9,977	2,503	25.08

From this table it will be seen that only 12 per cent. of the vaccinated cases died and most of the latter were among those revealing either poor or only fair scars. The percentage of deaths among the unvaccinated reached the high mark of 42 per cent. and the lowest fatality rate of 6 per cent. occurred among those whose vaccinal scar was good.

Let it be remembered that compulsory school vaccination only protects school children and does not necessarily insure a well-protected community. And even in the case of school children the laws are greatly neglected in many communities. The observations of more then a century and a quarter offer convincing proof of the differences in the incidence and number of deaths from smallpox in the vaccinated and the unvaccinated. Observe the number of deaths from smallpox in Germany, Sweden, England, Ireland, Scotland and in the Philippines and Puerto Rico where vaccination is more or less compulsory (except that the "conscience clause" in England diminishes the complete and full effect of the vaccination laws of that country). Compare this with the yearly toll of victims of smallpox in Austria, Russia, Spain, Turkey, the Balkan states and in those countries where no compulsory laws exist. The experience of France during the war period is worth mentioning. The French remembered only too well the serious epidemic of smallpox which swept over the country during the war of 1870-71, but during the great World War, the French army was efficiently protected by vaccination. The English, German and American troops were likewise protected. The movement of armies, prisoners of war and the increased migration of the civil population and refugees toward the latter part of the period of the World War

resulted in an uncontrolled and increasing spread of smallpox throughout Europe, the scourge being carried by those coming from Russia, the Balkan states, Turkey, etc. In many of the European countries today, a strict control against smallpox is practiced. Well-organized systems of inspection and complete machinery for the compulsory carrying out of regulations are available. This is lacking in this country. The experience in the Philippine Islands is so striking, that it should be brought to the attention of everyone. Before the American occupation thousands of deaths due to smallpox occurred annually. Manila alone contributed 6000 victims of smallpox to the annual mortality total. When the United States took possession of this territory and the federal government began immediate plans of introducing modern sanitary and health measures, vaccination was introduced. As its use was extended the number of deaths due to smallpox decreased. Approximately 19,000 fatal cases were reported in 1903 as against 239 in 1916 before the World War. At that time not all of the inhabitants were vaccinated. The possible danger of an epidemic of smallpox was minimized and attention was directed to more urgent health problems. However an exceedingly large number of unvaccinated Filipinos were roaming about, for when a slight outbreak occurred, it prevailed in epidemic proportions and this scourge in 1918 and 1919 killed 60,000 of the inhabitants. During the epidemic the American troops aided the sick and dying. Though fully exposed to the disease, only one case of smallpox occurred among these 5422 soldiers (all of whom were vaccinated).

Under the authority and jurisdiction of the League of Nations there was established after the World War a bureau for the service of epidemiological intelligence and public health statistics. This made possible for the first time in the history of mankind fairly accurate data concerning the number of cases of epidemic diseases in many countries, as the purpose of this bureau is to collect and interchange information concerning epidemic diseases. In its 1924 annual report dealing with 17 African, 20 American, 16 Asiatic and 29 European countries and Australasia, we find recorded a steady decline in the smallpox incidence after it having attained its peak in 1919 due to the effects of the war. In 1919, Italy reported 34,365 cases of smallpox but only 190 occurred in 1924. Similar declines are to be noted in most of the other European countries except England and Switzerland where the mild type of the disease prevailed. There were but

few cases of fatality in the latter, the result being late diagnoses, even concealment of the latter and an increasing neglect of vaccination. The records reveal 294 cases in 1919 in England and Wales and 3765 cases in 1924. In Switzerland, only 3 cases were reported in 1919 but 2126 cases in 1923 and 1234 cases in 1924 were recorded.

It is almost impossible to approximate the exceedingly large number of lives saved and the extent of misery avoided in the protection afforded by vaccination against smallpox. In spite of this there are some people who not only prevent the introduction of compulsory vaccination laws but are urging our legislative bodies to rescind the even partial compulsory vaccination measures in effect in this country as a protection against this dreaded disease. The prevention of smallpox depends primarily upon vaccination and secondarily upon quarantine, isolation and disinfection. The latter measures will check the spread of smallpox to a certain degree but successful vaccination and revaccination will usually prevent individuals from contracting this dreaded disease. Due to the fact that in recent years cases of severe smallpox have appeared but infrequently in this country and have been so mild in form as to play but a minor factor in mortality reports a false sense of security and even indifference appears to have been created. Observers in different parts of the world have also reported the outbreaks and wide prevalence of this peculiarly mild type of smallpox. In 1904, de Korté described such an epidemic in South Africa under the name of Amaas or Kaffirpox. In 1910, Ribas in Brazil speaks of a similar outbreak under the name of Alastrim, and similar observations in England, Switzerland, Australia and the West Indies Islands are recorded. The average individual when he thinks of smallpox has in mind only the severe forms with the dreaded lesions which leave the pitted scars. He does not seem to realize that just as in measles and other eruptive diseases, mild forms may occur more frequently than the severe cases. Mild strains of smallpox as mild forms of scarlet fever and other contagious diseases spread more diffusely than severe forms because their identity remains most frequently unrecognized, they are not taken so seriously by those attacked nor by the public at large, and the patient is usually not isolated, as he does not feel sick enough to remain in bed. When economic distress exists, the average individual is usually tardy in calling the family physician on the first sign of illness, so that when the latter does arouse suspicion, the infection has already spread to

others. Any of these unwise procedures defeat the purpose of properly enforcing health measures especially insofar as unreported and non-isolated cases lead to a rapid spread of contagious diseases. In the case of smallpox, the result has been a reduction in the extension of enforcing vaccination regulations and some communities have even displayed an indifference as to lessen to some extent the stringency of control measures against this scourge. It must be always kept in mind that smallpox in its old dreaded and fatal form has not been wiped out and that it is lurking around always at hand in a dormant state. No one knows when a case will light up and appear in our own midst and due to the fact that the vast majority of the medical practitioners of today have never seen a case of smallpox, the serious nature of the disease may remain unrecognized. Here we have at all times the focus for the spread of an epidemic, spreading like a wild fire in dry grass. Many concrete examples could be cited having occurred even within the past few years. In 1922 in Denver there were 805 cases and 247 deaths (a fatality rate of 30 per cent.) due to smallpox. In November 252 cases were reported, and on the 21st of that month an order requiring persons to be vaccinated was issued. The following month only 81 cases were reported. In 1921, an outbreak in Kansas City resulted in 1090 cases and 222 deaths, and the epidemic abated only after 200,000 people were vaccinated. In April, 1931, six cases of smallpox occurred among the colored residents of Newark, N. J. The disease had existed for some weeks before a correct diagnosis was made and the city health department was able to combat its spread. However within a few weeks after the cases were discovered over 37,000 persons were vaccinated. The one and only control and best assurance which we have at our disposal to avoid in most instances an attack of this disease and becoming a menace to oneself, to our immediate dear ones and to the community, is the precautionary measure of universal vaccination and revaccination. Until recently (1932) more than 30,000 cases of smallpox were reported annually in this country. It is true that in 1932, 1933 and 1934, there was less of this dreaded disease reported than previously, though in the latter year there was a slight rise over 1933. Significant however is the fact that most of the smallpox cases reported by American states previous to or since 1932 occurred in the main in those states in which the sentiment has been opposed to compulsory vaccination. We must keep constantly before us the fact that for almost four

decades a mild form of smallpox has been increasingly prevalent in the United States and surrounding countries, with a fatality of about 0.1 per cent. being recorded among the unvaccinated. From time to time outbreaks of the more severe forms of the disease have occurred and are always a possibility, the fatality rate among the unvaccinated having reached as high as 30 per cent. (as noted above). Let us also remember that the movements of travelers coming from other lands where cases of smallpox may be found or severe epidemics have occurred and where universal or mass vaccination is practiced but indifferently if at all makes possible at all times the appearance of smallpox at our very doorstep and even the appearance of severe epidemics. I wonder what unpleasant results among these lines will occur when aeroplane travel between this and South American countries and Mexico becomes more common. It is also of import to note that during periods of economic depression there is generally a decline in the incidence of the number of cases of smallpox due in the main to a decrease and even a standstill in the movements of laborers coming from rural districts into large cities. This happened during the short 1921-22 period of economic depression. There was recorded an increase in the incidence of smallpox during the prosperous period of 1920, and later in 1924 and 1930. We are now experiencing another decline, but with the return of prosperity what does the future hold forth as to an increase of the incidence of smallpox? Such forces as the importation and even smuggling of Mexican laborers into our country or the movements of negroes and migrant laborers from unvaccinated rural regions into populated cities may bring about epidemics of this dreaded scourge. Vigilance is needed, but better still national protection is possible at all times by mass or universal vaccination. Our educational endeavors must be intensified in the direction of extending compulsory vaccination laws and making everyone conscious of the fact that unless a more effective method of protection against this scourge is made available, vaccination must be practiced to insure safety and better health for humans. Quarantine, isolation and disinfection alone will not prevent or stop epidemics of smallpox. Each and every individual in a community should be vaccinated and revaccinated (if necessary) for personal safety and in the interest of protecting others in the community. Compulsory legislation for smallpox vaccination is justified. Mention should be made that there are many states which have laws or regulations providing for or

authorizing vaccination at public expense, the classes of persons entitled thereto varying in the different jurisdictions, though in most cases it includes the general population.

VACCINE VIRUS

Vaccine virus can be obtained from human sources, but the latter is rarely employed today due to the fact that the supply would not be sufficient, and the "arm-to-arm" vaccinations also present the possible danger of transmitting other human diseases. In some countries however the use of the human virus in the arm-to-arm vaccination technique is still practiced. It was in 1860 that vaccination with the "animal lymph" of calves came into more general use, although it was employed more or less since the time of Jenner. Since 1866 when the Beaugency strain was discovered and especially after 1891 when glycerin was employed for purifying and preserving it, the "Bovine Virus" was and is employed mainly for the yield of the present-day smallpox vaccine. This makes possible a constant fresh supply and in amounts as may be required. The animals in general use for the preparation of vaccine virus are young, carefully selected calves, preferably females (though this is immaterial), but they must be at an age of from four months to one year. The younger animals are easier to handle. They are kept under rigid veterinary observation and supervision for a few weeks previous to and during their actual treatment to insure freedom from disease, the tuberculin test also being carried out, and any reactors are eliminated. The calves are kept under the best sanitary conditions which can meet all known scientific exactness for the latter. The healthy animals which are to produce the smallpox vaccine of the market are treated (vaccinated) under aseptic conditions with a previously prepared virus which is known to be active (and designated as the "seed" virus). After the typical vaccinia vesicles develop (usually six or seven days after vaccination), the entire contents of the latter including the serous fluid or lymph and pulpy exudate (but minus the crusts which are removed) are collected under rigid aseptic conditions, employing humane operative procedure. The pulpy mass is ground thoroughly under aseptic precautions in a special mill making an even emulsion with four times of its weight of 50 per cent. glycerin containing 1 per cent. carbolic acid. This finished mixture is stored for three to four weeks at very low temperatures to permit bacteria which may be present to die. Every lot of vaccine is then subjected to rigid bacteriological and toxicological examinations to insure a preparation

free from all disease-producing organisms and toxic substances. Autopsies of the calves employed in preparing the marketable virus are made, and no virus is used until necropsy reports reveal that the animals were in perfect health. The preparation is then tested on rabbits and susceptible humans to prove that the virus yields a successful "take", the actual strength or potency being estimated from the speed of the development and the extent of the subsequent reactions. After these operations and tests are conducted exercising every possible care, the preparation is filled under rigid aseptic conditions in sterile capillary tubes and released for the market. The sterile capillary tube is the only form of dispensing allowed in this country. A calf usually yields about 10 grams of pulp which when made up will produce material to vaccinate about 1500 children.

KEEPING SMALLPOX VACCINE

Smallpox vaccine, so-called vaccine virus, cannot be injured by freezing. The U. S. Public Health Service requires that the date of expiration be marked plainly on each package (marketed). This indicates the expectancy of potency (efficiency) when kept under favorable conditions. The colder the temperature, the more assured will one be of the efficiency of the product. It should be kept well below freezing if possible. Tests have shown that a potent vaccine refrigerated constantly at 10° F. will retain its activity for four years. Kept at 50° F. (or 10° C.), the temperature of the ordinary house refrigerator, the potency remains for from three to four months, while at room temperature (7° F. or 21° C.), (in a drawer, case or bag) the average life of vaccine virus is from one to three weeks and the number of "takes" is reduced to 50 per cent. If the vaccine virus should be placed in one's vest pocket or close to the body or exposed to summer heat, its complete value will be lost within three days and "takes" will not result. Kept accidentally near a stove, radiator or near steam pipes as might happen during delivery or mailing when packages are carelessly thrown about and where temperatures may approximate 120° to 140° F. (or 49° C. to 60° C.), the potency will be destroyed within five minutes. Once the strength or activity of vaccine virus is destroyed or weakened, it cannot be restored by any known treatment. It is therefore usually advisable to obtain from the manufacturer the smallest practical amount which may be needed at any one time, unless below freezing temperatures for keeping the smallpox vaccine is available or possible.

OTHER IMPORTANT FACTS CONCERNING VACCINATION

If you have never been vaccinated, you should do this at once. Vaccination of infants is attended with less outward effects and possible complications than that of older children, so that vaccination should be performed before the child reaches one year of age and as soon after birth as practicable, preferably before teething. Avoid vaccination in the presence of eczema and especially when acute infections of the central nervous system are particularly prevalent. Vaccinate if possible during the cool weather, the late fall, winter and early spring (October to May) being the most suitable seasons. Not only is the quality of the vaccine likely to be better during the cold weather, but during the latter period children are less apt to play with bare arms or legs and thus the possible risk of infecting the vaccination wound is reduced to a minimum. Vaccination on the arm (outer surface of the left arm at about the insertion of the left deltoid muscle is most suitable) is to be preferred. In leg vaccinations (especially with babies in diapers and with young children) the wounds are exposed to more moisture, to greater contamination from street dust, and to possible injury and subsequent complications. If the leg is selected, the site chosen should be on the calf below the head of the fibula and not on the outer surface of the thigh.

Vaccination is a simple operation, yet one which requires some skill in performance and care in after treatment. Any method may be employed providing however that the vaccine is deposited in the deeper layers of the epidermis (superficial skin) covering a small area, not larger than ⅛ inch in any direction, and avoiding the drawing of blood or any marked irritation of the skin. The method of incision or linear abrasion, the drill method and best of all the multiple pressure or multiple puncture method are employed. When using either of the first two methods, the arm after vaccination should be exposed to the air (BUT NOT TO DIRECT SUNLIGHT) for one-quarter of an hour before the clothing is allowed to touch the dry area. In case of the multiple pressure method, the remaining glycerinated vaccine can be wiped off immediately, and with this method "control" sites are not necessary as when other techniques are employed. In preparing the site for vaccination, the skin in the area to be treated is thoroughly cleansed with soap and water or with alcohol or preferably with acetone on sterile cotton or gauze and then wiped dry. In vaccinating, antiseptics or even soap are not necessary, but if used, all traces of the latter are to be removed with boiling water from the area to be treated

and the latter is then dried; or if a volatile antiseptic is used, such chemical agent should be allowed to evaporate. Not only heat, but antiseptics also kill or reduce the potency of vaccine virus. Injury to the vaccinated arm should be avoided. Tight sleeves or any tight covering which tend to macerate and inflame the tissues during the "take" should not be allowed. Do not use pads, plasters, adhesive or "vaccination shields" (made either of celluloid, felt or similar material), as they act as a poultice, and thus gather heat and moisture, to objectionable features. The wound should be kept clean, cool, and dry. It is best to wear a loose-sleeved white garment. The best dressing is the unbroken skin and the scab which subsequently forms. If dry sterile gauze is applied for the first few days after vaccination, this should be removed before the pustules appear.

SUCCESSFUL VACCINATION

Vaccinations should always be inspected to be assured of a successful "take," which in turn is an assurance that the individual is protected against smallpox. It is of interest to note that an immunity is also produced against cowpox.

Smallpox Vaccine Virus of FULL POTENCY when applied (by any of the techniques) to the skin incites a localized and mild form of the disease (cowpox) from which the patient recovers rapidly. The types of reaction following vaccination and the immunity (resistance or protection) created can be judged and indicated only if vaccine virus of full potency was used. Where there is an absence of immunity to smallpox prior to vaccination, the reaction produced is spoken of as a typical PRIMARY VACCINATION OR VACCINIA. One or more small, round, red, hard papules appear at the site of inoculation within a few days. These become vesiculated on the fifth day and are surrounded by a zone of redness (or areola), which may appear on the following or within a few days; and though rather narrow from the third to the seventh day it begins a sudden spread on the seventh day after vaccination and reaches its maximum in from eight to fourteen and usually in nine to ten days. There is generally but one vesicle, clear and pearl-like surrounded by a deep, red, and even swollen areola, a picture of the "pearl upon the rose leaf." The skin may feel hot and be painful. The auxiliary nodes or glands may become enlarged and tender. Soon after the tenth day the areola (or erythema) begins to fade, the swelling subsides, and on the following day the pustule dries rapidly, becomes brown and crusted, the wrinkled scab separating and dropping off in two to three weeks (usually about the

twentieth day). Systemic symptoms and indications of a mild febrile reaction may appear, but they disappear quickly. In highly susceptible patients, a rash covering a large portion of the body may develop (eruptive vaccinia), but disappears quickly.

If the patient has some degree of or partial immunity as would be the case in an individual who has partially lost the protection gained from a previous vaccination or an attack of smallpox or natural vaccinia, a modified or accelerated reaction, known as vaccinoid, results when vaccination is practiced. The reaction is less severe and develops more quickly, reaching the maximum in from three to eight days. A vesicle is generally found at the center of the reaction. Scars left in cases of vaccinoid are much less marked.

In highly immune individuals, as would be found in persons fully protected against smallpox by recent vaccination or a previous attack of smallpox or cowpox, the maximum diameter of the erythema is reached and passed in from eight to seventy-two hours. There is usually no vesicle and scars are not usually produced. It is of interest to point out here that in various parts of the United States, mild smallpox has been prevalent among the unvaccinated and the condition was diagnosed as "chicken pox." Such individuals will give no evidence or history of previous successful vaccination or attack of smallpox. Subsequent vaccination will yield the immune reaction described here.

The three types of successful vaccinations (primary vaccinia, vaccinoid, and immune reaction) are an arbitrary differentiation based on the time when the maximum diameter of the erythema (broadest redness) is reached. It is therefore important to observe and measure (if necessary) at intervals of two days after vaccination the diameter of the redness. The co-operation of the person vaccinated may be needed to observe when the maximum reaction is obtained. There appears to be a definite relation between the immunity conferred and the diameter of the erythema when at its maximum in the area of the local eruption; and furthermore the degree and duration of the immunity are directly proportional to the typical nature of the "take" (being assured of course that a potent vaccine virus and the proper technique were used in vaccination). The amount or degree of redness and the time of the first appearance of the latter during vaccination are not a measure of the state of immunity in the subject. The QUICKER the maximum reaction is attained and then subsides, the greater is the immunity which prevails. It is therefore the TIME which is required

for the area of redness to reach its MAXIMUM which serves as the index of the existing immunity.

NON-TAKE

It is a fallacy to state, and yet such statement is frequently quoted that if a vaccination fails, the subject is immune. The eminent Sir William Osler though repeatedly vaccinated never had a successful "take." Supposedly an immune, he worked hard in the smallpox wards in the Montreal General Hospital and also mingled freely with friends and relatives. It was in December, 1875, he himself contracted the dreaded malady (though a mild attack), and in the years to follow he always cited his own case to illustrate the fallacy of the "non-take" belief as an evidence of immunity which prevailed at that time.

Every vaccination, if performed properly (preferably multiple pressure method) and with a fresh and potent vaccine virus, should give a reaction as indicated previously. If the papule and areola do not appear until the fourth day and there is no vesiculation, either the technique was unsatisfactory or more than likely a weak vaccine virus was used. In case there is any doubt as to the potency of the virus, either use another fresh virus which has been kept cold or employ one of known potency. If this is not possible, then to guard against failures, vaccination should be performed at more than one site at least an inch apart, keeping each area of the minimum size. The failure of a vaccination to "take" does not indicate a protection against smallpox. Differences in skin receptivity, independent of the existence of an immunity, are known to exist. It has been observed that some very young infants are not as easily vaccinated successfully as are most of the older children. However they have been found susceptible to smallpox. In still rarer instances, some individuals have been found resistant to specific batches of vaccine virus, the latter generally yielding successful "takes" in others. In both instances vaccinations with potent lots of vaccine virus should be repeated until "takes" are successful.

RE-VACCINATION

It is possible for some non-immunized individuals to be exposed to smallpox, especially to the milder forms, without contracting the disease. This is not however a definite evidence of the existence of an immunity. A successful vaccination especially if recent will protect almost entirely against smallpox. If the successful vaccination had been performed only once previously and a long period of time has elapsed before exposure to an outbreak of a severe epidemic, contraction of the dis-

ease, if at all, will result in a suppression of fatal and serious symptoms and smallpox only in a mild form will prevail. The possibility of contracting smallpox varies with the intensity of the exposure, with the severity of the strain of smallpox to which one is exposed, and with the susceptibility of the individual. It is impossible to attempt to fix a definite time for the duration of an immunity conferred by a successful vaccination. This varies as in other infectious processes. It is a known fact that the immunity wears off after a number of years, being absolute for the first few years, beginning to disappear two years after vaccination; and in most cases, it is almost completely lost after a ten-year period (average duration of immunity is regarded as seven years). In this as in other diseases immunity is a relative term.

Health officers who are continuously exposed and those living in areas where smallpox is prevalent need more frequent vaccination than those who are not exposed to this disease. For the public at large in this country, two successful vaccinations are usually advised and are regarded as being sufficient to protect for life against the milder forms of smallpox which are the types most prevalent in this country. The first successful vaccination is to be performed before the child reaches one year of age or as soon after birth as practicable, preferably before teething (at age of eight months if convenient), and this should be repeated seven years later or sometimes during the first few years of attendance in school. If there may exist a particular danger of exposure to smallpox and especially to the severer forms, all persons should be vaccinated at least every five years, as is done in Japan.

Successful vaccination and revaccination (even only once) performed systematically confer complete protection to a community against all forms of smallpox. Even though individual protection may vary, the communal protection against this scourge is practically absolute. A person successfully vaccinated and revaccinated who later is exposed to a severe form of smallpox and contracts the disease has the latter in a much less severe form than unvaccinated persons. The result is that vaccination eliminates completely the milder forms of this disease, and not only reduces the incidence rate, but lowers markedly the death rate of the severe forms of smallpox.

DANGERS FROM VACCINATION

The fear of vaccination and the alleged dangers due to this procedure have been greatly magnified and have no basis in fact if simple precautionary measures of cleanliness are observed. Even a pin prick or a knife cut may result in harmful after effects. We must of course remember that

a slight but nevertheless an open wound is produced during vaccination. If a clean or aseptic technique is not used, or if the wound is neglected and dirt gets in, or if unclean dressings are applied, complications and even tetanus as in the case of any other wound may arise. Vaccination wounds in infants are rarely infected and in children, they are more likely to become contaminated if the latter are running about or the wounds are freely exposed as during the summer months. Cleanliness is absolutely essential and this will result in the complete elimination of possible septic infections and tetanus.

Autovaccination is the result of the scratching of the virus with the fingers and transferring it to the mucous membranes of the nose, mouth or any part of the skin. Vesicles at these distant places may thus appear. Introduced into the eye, blindness may result.

With the present technique of vaccination where dressings are avoided and the insertion of the vaccine virus is restricted to a very small and superficial area, thus insuring the rapid drying of the vesicle and the primary vaccination is performed in most instances in early infancy, it is exceedingly rare to hear of tetanus or demyelination encephalomyelitis causing complications during vaccination, neither due to the vaccine virus itself.

The possible dangers connected with vaccination where the proper technique is employed are infinitesimal as compared with the benefits derived. If vaccination was made compulsory and was rigidly followed, smallpox would be unknown. It exists in this world, due to the unvaccinated who are a detriment not only to themselves but to everyone in the community.

DIPHTHERIA

The disease we term diphtheria occurred in ancient times and can be traced under various names to the Homeric period of Grecian history. The "Askara" or "Serunke" of the Hebrews of ancient times is regarded as the same condition known today as diphtheria. This disease justly regarded even today as a dreaded scourge was so much feared by them that the first case located in a community was sufficient to proceed and sound a warning with a blast of the shofar, though generally the latter was sounded only after the appearance of the third case of other infectious diseases.

Arataeus, the Cappadocian, one of the most prominent of the early Greek clinicians and medical author of note who described diseases in admirable Ionic and who practiced in a Roman province in Asia Minor during the second century A. D., gives a classic account

of the Egyptian disease or the Egyptian sore throat and Ulcera Syriaca (Syrian ulcer), the name by which he presents a clinical description of what is recognized today as diphtheria. This is the first worthwhile description of this malady to appear in writing. Äetius of Amida, a royal physician and lord high chamberlain at the court of Byzantium during the sixth century A. D., gives an interesting description of epidemic diphtheria. The latter is spoken of as "esquinancie" in the Chronicle of St. Denis (580). Hartmann Schedel, city physician of Nuremberg, gives a vivid description of an epidemic of diphtheria in his home town in the year of 1492. From 1581 to 1600, six epidemics of this disease appear throughout Spain and then spread to Italy. Nicolas Gutierrez de Angulo (1444-1522) described diphtheria under the name of Garrotillo (Tratado de la enbermedad del Garrotillo), and as such descriptions were given by Fontecha (1611), Villa Real (1611), Herrera (1615) and others. As the "nawe krannckheyt" diphtheria is described as a new disease in Codex 11548 of the Vienna Hofbibliothek (fol. 278 verso). Epidemics in Italy occurred in 1611 and from 1618 to 1630; and Spain was revisited in 1630, 1650 and 1666 with outbreaks of diphtheria.

The distinguished English diagnostician William Herberden (1710-1801) in his Commentaries gives a detailed clinical description of diphtheria, mentioning the diminished liability to this disease after adolescence. John Fothergill (1712-80) presented original descriptions of diphtheritic sore throat. It was Pierre Bretonneau (1771-1862) prominent French internist who gave the present name diphtheria to this scourge in his illuminating essay (Des inflammations spéciales du tissu muqueux et en particulier de la diphthérite, Paris, 1826). Edwin Klebs (1834-1913), professor of pathology at various institutions in Germany and later at Rush Medical College in Chicago, was the first to see and describe the diphtheria bacillus in 1883. He mentioned the constant occurrence of the latter in the pseudomembranes from the throats of those having the characteristic symptoms of diphtheria. One year later Friedrich Löffler (1852-1915) professor of hygiene at Greifswald, definitely established the causal relation of the diphtheria bacillus (1884), separated and isolated it from other bacteria, and differentiated it from the organisms causing the disease in calves and doves. It is on this account that the diphtheria bacillus is designated at times as the Klebs-Löffler bacillus.

In this country an epidemic in 1659 at Roxbury, Massachusetts, which spread throughout New England and was referred to as

"Cymanche Trachealis, or "bladder in the throat," is regarded the same as diphtheria. The Legislature of Connecticut ordered a day of thanksgiving in 1662 upon the cessation of a similar epidemic, and other legislatures also decreed days of thanksgiving at the cessation of such epidemics. Under the name of angina ulcusculosa, Dr. William Douglass of Boston gives an excellent account of an epidemic of diphtheria in that city during 1735 and 1736. The ravages of the disease were fearful and it came to be known commonly as "throat distemper," "putrid and ulcerous sore throat," "gangrenous ulcer," and "the plague among children," as in some of the epidemics, very few children escaped; and it attacked the young even in uninhabited areas where there wasn't an apparent possible communication with the sick. Diphtheria was known for its highly contagious character and the fatality rate among attending physicians was exceptionally high. In spite of all available medical knowledge of days gone by and the best of attention, there was but little which could be done for cases of diphtheria and but few diseases caused such shudders of horror or presented such high mortality. Epidemics were reported in the northern colonies in 1742, 1755, 1775, and 1787. John Kearsley, Jr., who had a troublous career because of his violent Tory opinions and who was among the organizers of the Philadelphia Medical Society (1766), published in 1769 in the *Gentleman's Magazine of London* an article on the epidemics of malignant sore throat ("angina maligna"), which had occurred in Philadelphia in 1746 and 1760. This is said to have been the first American medical contribution to a foreign periodical. John Ogden, a medical practitioner in Jamaica, Long Island, addressed a communication in 1769, printed later in the *Medical Repository of New York,* on the "Malignant Sore Throat Distemper." An article on the "Observations on the Angina Malignana; or the Putrid and Ulcerous Sore Throat, with a Method of Treating it, by a Lover of Pennsylvania," appeared in 1769. John Kearsley, Jr., or Benjamin Rush is supposed to have been the author. An essay by Samuel Bard (1742-1821), a native of Philadelphia, who became well known as a medical practitioner in New York City, on "angina suffocativa," or "sore throat distemper" (1771), in which he advanced strong reasons for believing that membranous croup and pharyngeal diphtheria were different manifestations of the same disease, is mentioned by Sir William Osler as "an American classic of first rank." Richard Bayley (1745-1811), prominent surgeon and anatomist of New York City,

whose dissecting room was the focus of the famous "Doctor's Mob Riot" in 1787 (the result of ignorant prejudice against the dissection of the human body), presented in 1781 in a letter to Dr. William Hunter, "Cases of the Angina Trachealis with the Mode of Cure." Much discussion prevailed during the colonial period concerning "Angina Suffocativa or Trachealis." In this country, throughout the nineteenth century, great epidemics of diphtheria spread through populated areas, especially in the larger cities. Such epidemics were found and reported in the larger communities, and epidemic waves recurred at five and ten-year intervals. The death rate in days gone by ranged between 20 and 60 per 100,000 and during periods of epidemics reached well over the 200 figure. Children are the ones most defenseless against this disease, and quite naturally this scourge has been particularly a school disease spreading among children when congregating in large numbers in any environment. With the general improvement in sanitation, and the increasing use of modern methods of control, there has been a prolonged continued decrease in the incidence of diphtheria. These measures and more adequate methods of treatment have resulted in a decreased mortality during the past five or six decades to ten and even twenty fold. Death rates of cities for the past forty years, or since the discovery of diphtheria antitoxin, produce valuable information for study. Herewith follow compilations for the two largest cities of the Commonwealth of Pennsylvania, the largest cities in the States of New York and New Jersey, and there is also included the death rates from diphtheria in the City of Camden, N. J.

DEATH RATES FROM DIPHTHERIA (INCLUDING CROUP) PER 100,000 POPULATION.

	1890	1895	1900	1905	1910	1915	1920	1925	1930
Camden, N. J.	94.0	99.0	4.0	9.0	14.0	19.0	24.0	29.0	
Newark, N. J.	110.4	79.1	46.7	30.1	23.3	14.6	9.7	14.5	10.8
New York City	134.4	85.8	58.0	40.0	28.0	21.8	14.0	10.7	2.9
Pittsburgh, Pa.	86.4	32.9	36.9	20.4	29.3	22.3	20.1	11.5	8.5
Philadelphia, Pa.	119.4	100.6	50.0	34.1	24.6	22.7	16.7	11.8	2.5

The death rates from diphtheria for the entire country during the past quarter of a century reveal a steady decline due to modern scientific weapons. The number of deaths per 100,000 of population in the United States were:

1910	1915	1920	1925	1930
21	16	15	8	5

Individuals need not be kept any longer in dread of this scourge, for there is no reason why children should have diphtheria today. There is not a disease afflicting mankind which is so thoroughly understood by modern science as diphtheria. Accurate and simple methods of bacteriological diagnosis are available to detect suspicious cases as well as carriers of diphtheria. There is available a test which makes possible the detecting of those who are susceptible to this disease, so that one can determine accurately whether a child is in danger of contracting diphtheria if exposed to it. If stricken, a specific remedy for the sick one is always at hand which if used early and properly makes recovery almost certain. Methods of protecting permanently against diphtheria by simple treatments and procedures of proven value can eliminate this disease as a scourge of children. Modern science has won the victory over this once dreaded infection, but the wholehearted co-operation of everyone is needed in this warfare to aid in making the danger of diphtheria practically negligible.

THE DISEASE AND ITS CAUSE

Diphtheria is caused by the growth of a specific microörganism, the diphtheria bacillus, on the membranes of the surface of the mouth, throat, larynx, windpipe, or nasal passages. Once the organisms or bacteria gain a foothold, they multiply rapidly and form the so-called "pseudomembrane" which is usually grayish white in color. There is frequently marked mechanical disturbance and mechanical injury caused by the local inflammation. In days gone by when the use of antitoxin and the present-day vigilance in examinations were lacking, it was a frequent occurrence to find laryngeal obstruction in children due to an extension of the infection downward into the larynx with membrane formation. It was not infrequent for death to result due to suffocation. When once established in the throat, the diphtheria bacilli (all varieties) produce large amounts of a powerful poison (so-called toxin) which is thrown off into the surrounding tissues, and this toxin is subsequently absorbed into the blood stream and carried throughout the patient's system. Most of the generalized symptoms and harmful and alarming character of the disease and especially the severe systemic disturbances are due to this soluble and diffusible poison or toxin elaborated by the bacilli. The organisms themselves in the main are found during the infection only in the local affected area. The duration of the disease is variable being from a few days to several weeks and even months, especially in the cases of nasal diphtheria. This infection is comparatively rare in the Tropics. It seems

to be found mainly in temperate climates and though present during every month of the year, it prevails most commonly during the colder months, the incidence of diphtheria being nil during the summer months.

HOW DIPHTHERIA SPREADS

Diphtheria is transmitted from one individual to another directly or indirectly by contact or droplet infection (as in spitting, coughing, sneezing, loud talking, etc.). Kissing and the use of infected toys, pencils, eating and drinking utensils and soiled bedding or clothing of a diphtheria patient or carrier may be responsible for the passing of the organism from one to another. It has been found that individuals may retain toxic diphtheria bacilli in their nasal passages and throat for long periods after recovery from the disease. The latter individuals as they are recovering are known at times as "convalescent carriers". But there are quite a number of persons harboring the bacilli in their throats and adjacent areas who appear in good health and have never given evidence of an attack of diphtheria. Such individuals are known as "contact carriers". Both groups may be transient (temporary) carriers or chronic carriers. It is these seemingly healthy persons who as carriers are definite menaces and are most likely the important cause for the existence of the disease (diphtheria) in modern communities. Less important, though still of some significance, is the possible transmission by infected food and also the fact that outbreaks of diphtheria have not been uncommon where milk was the vehicle of transmission for the infection. The bacilli may find their way into the milk either because of the presence of a case of diphtheria (perhaps a mild one) or due to the contamination from a milk handler who is a diphtheria carrier. The first epidemic of this disease traced to milk occurred in 1877, in Sutton, England, and was reported by Dr. E. J. Jacob. The following year, an outbreak of 264 cases was reported in London by a Mr. Power, all traced to the same milk supply. During the same year three other outbreaks traced to milk were reported by Dr. Jacob. In 1889, the bacilli of diphtheria were cultivated in milk by Klein and ten years later (1899), Gowhill, Eyre and Klein isolated the diphtheria organisms from city milk supplies (not pasteurized). In the bulletins of the Public Health Service there are recorded over a period of years epidemics of 960 cases of diphtheria produced by unheated cow's milk.

(*To be concluded in October issue.*)

A NOTE ON THE DETERMINATION OF VANILLIN WITH 2,4-DINITROPHENYLHYDRAZINE

By Nathan Rubin and Albert Bloom

AS a preliminary step in conducting an investigation in this laboratory, it was necessary to determine the accuracy with which vanillin could be determined gravimetrically as its 2,4-dinitrophenylhydrazone.

Iddles and Jackson (1) reported high results by this method (Av. + 2.18%); using a technique that had been derived by working with benzaldehyde. A study of this method showed the following, any or all of which may have accounted for the poor results.

a. The solution of the carbonyl compound was added to a large excess of the reagent.

b. The precipitate was dried over concentrated sulfuric acid in a partial vacuum.

c. The conditions that gave good results with benzaldehyde need not necessarily be directly applicable to vanillin.

The following method was found to give satisfactory results in the hands of the authors.

The sample of vanillin was dissolved in 20 per cent. alcohol. An aliquot of this was taken and diluted with water to about ninety (90) cubic centimeters and the reagent slowly added with constant stirring. The reaction mixture was allowed to stand the indicated time and the precipitate collected in a weighed Gooch crucible, washed with 40 cc. of 2N. hydrochloric acid, then with 10 cc. of water and finally dried to constant weight at 105° C. All of the reactions were carried out at room temperature. The filtrates from the reaction mixtures showed no turbidity after standing one hour.

The reagent was prepared by triturating 0.4 gm. of 2,4-dinitrophenylhydrazine with 21 cc. of concentrated hydrochloric acid and then diluting to 100 cc. with water. After standing 24 hours it was filtered just before use.

Wt. Vanillin Gram	Mole Reagent Mole Vanillin	Total Vol. Cc.	Time of Standing Min.	Recovery %
0.0600	1.5	130	30	99.65
0.0600 (a)	1.5	130	30	99.11
0.0600	1.5	250	30	99.65
0.0605 (b)	2.	250	30	99.88
0.0605	2.	150	15	98.98
0.0605	1.5	150	60	99.35
			Av.	99.44

(a) 10 per cent. of alcohol added to reaction mixture.
(b) 0.02 gm. of coumarin added.

Conclusion

A method for the gravimetric determination of vanillin as its 2,4-dinitrophenylhydrazone, which gives satisfactory results even in the presence of 10 per cent. of alcohol is described.

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REFERENCE

(1) H. A. Iddles and C. E. Jackson, *Ind. Eng. Chem. Anal. Ed., 6,* 454 (1934).

Vitamin B1 Synthetic

All the higher plants synthesize vitamin B1 and presumably utilize it as part of their life cycle processes. All animals need it in their life processes but strangely enough are unable to make it. The operation of extracting it from plants is laborious and expensive. The artificial synthesis recently accomplished is by means wholly different than those which the plants utilize.

The synthesis is effected by combining 2-methyl-5-brom-methyl-6-amino-pyrimidine with 4-methyl-5-beta-hydroxy-ethyl-thiazole. The former is somewhat related to the hypnotic barbital; the latter is a pyridine-like sulfur containing substance more or less akin to certain of the agents used in accelerating the vulcanization of rubber and in the sensitization of photographic plates. Each of these, however, is a new substance and every atom must be in its proper place. Both of these products used in the synthesis are built up by numerous steps from simple molecules through complicated procedures. Each step adds a structural feature of the molecule till the whole is complete and duplicates the end product of nature's art. In spite of the difficulty of the synthesis, the vitamin can be produced much more cheaply by this process than by extraction from natural products. (Research Corporation datum.)

BALSAM PERU—THE U. S. P. XI TEST FOR ROSIN

By S. Parnas and R. E. Schoetzow

THE United States Pharmacopœia XI appears to be in error, in that it directs that in testing Balsam Peru for Rosin, the sample be extracted with xylene instead of petroleum benzin.(1) The U. S. P. XI Rosin test is worded as follows:

> "In testing for rosin as an adulterant in resins, gum resins, and balsams, unless otherwise directed, place in a small mortar 1 Gm. of the substance, powdered or crushed if necessary, and add 10 cc. of purified petroleum benzin unless the substance contains free cinnamic or benzoic acid, in which cases the petroleum benzin should be replaced by xylene. Triturate well for one or two minutes, filter into a test tube, and add to the filtrate 10 cc. of a fresh aqueous solution of copper acetate (1 in 200). Shake well and allow the liquids to separate: the benzin or xylene layer should not show a green color (rosin)."

Since Balsam Peru contains free cinnamic acid, the use of xylene is indicated.

The German (2) and the Swiss (3) Pharmacopœias direct that petroleum benzin be used in this test. Allen's Commercial Organic Analysis (4) mentions the use of petroleum benzin, but not xylene. Our work indicates that petroleum benzin and not xylene should be used, and that the testing method for rosin in Balsam Peru, in the United States Pharmacopœia should be revised.

In recent years we have not encountered any Balsam Peru which will comply with the xylene modification. This material, although submitted to us as being of authentic origin and unadulterated, does not comply with the test as described in the U. S. P. XI using xylene, but does comply if petroleum benzin is used. To show that such Balsam Peru is free or practically free (1% or less) of rosin and that the petroleum benzin modification does detect such an amount, numerous tests were performed; the results are presented in the following table:

Material Tested	Solvent	Color produced in Solvent Layer by Copper Acetate Solution
Balsam Peru (1 Gram)	xylene	green
Balsam Peru (1 Gram)	petroleum benzin	colorless
Balsam Peru (1 Gram), plus 0.05 Gram rosin, plus 0.1 cc. alcohol (a)	petroleum benzin	dark greenish-blue
Balsam Peru (1 Gram), plus 0.01 Gram rosin, plus 0.1 cc. alcohol	petroleum benzin	faint greenish-blue
Balsam Peru (1 Gram), plus 0.1 cc. alcohol	petroleum benzin	colorless
0.01 Gram rosin, plus 0.1 cc. alcohol	petroleum benzin	light greenish-blue
0.12 Gram cinnamic acid, plus 0.18 Gram benzoic acid, (b) plus 0.5 cc. benzyl alcohol	petroleum benzin	practically colorless
0.12 Gram cinnamic acid, plus 0.18 Gram benzoic acid, plus 0.5 cc. benzyl alcohol,	petroleum benzin	decided greenish-blue
plus 0.01 Gram (1%) rosin 0.12 Gram cinnamic acid, plus 0.18 Gram benzoic acid, plus 0.5 cc. benzyl alcohol, plus 0.05 Gram rosin	petroleum benzin	very strong greenish-blue
0.12 Gram cinnamic acid, plus 0.18 Gram benzoic acid, plus 0.5 cc. benzyl alcohol	xylene	strong greenish-blue
0.12 Gram cinnamic acid, plus 0.18 Gram benzoic acid, plus 0.5 cc. benzyl alcohol, plus 0.01 Gram rosin	xylene	strong greenish-blue
Balsam Peru (1 Gram), plus 0.5 cc. benzyl alcohol, plus 0.1 cc. alcohol	petroleum benzin	colorless
Balsam Peru (1 Gram), plus 0.5 cc. benzyl alcohol, plus 0.1 cc. alcohol, plus 0.01 Gram rosin	petroleum benzin	faint greenish-blue

(a) 0.1 cc. alcohol was introduced so that the rosin might be thoroughly incorporated.

(b) The mixture was made to contain the amounts of benzoic and cinnamic acids which are found in 1 Gram of Balsam Peru.

Material Tested	Solvent	Color produced in Solvent Layer by Copper Acetate Solution
Balsam Peru (1 Gram), plus 0.5 cc. benzyl alcohol, plus 0.1 cc. alcohol, plus 0.05 Gram rosin	petroleum benzin	strong greenish-blue
No sample— Blank on copper acetate	xylene	colorless
No sample— Blank on copper acetate	petroleum benzin	colorless

The above tabulation of tests shows that xylene is not suitable as a solvent, since it will dissolve enough cinnamic or benzoic acid to give a positive test with the copper acetate T. S., and that xylene should not be used in the pharmacopœial test. The tabulation also shows that petroleum benzin will not extract enough cinnamic or benzoic acid to give a false test as does the xylene. It also shows that petroleum benzin will detect quantities of rosin as small as one per cent. in Balsom of Peru.

We conclude, then, that the U. S. P. XI rosin test, in as far as it refers to Balsam Peru, should be revised, so that the use of xylene is no longer required.

REFERENCES

(1) *Pharmacopœpia of the United States,* Eleventh Edition, page 465.
(2) *Deutsches Arzneibuch,* Sixth Edition, page 85.
(3) *Pharmacopoea Helvetica,* Fifth Edition, page 151.
(4) *Allen's Organic Analysis,* Fifth Edition, Volume 4, page 329.

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SCIENTIFIC AND TECHNICAL ABSTRACTS

Compiled by Linwood F. Tice, M. Sc.

[EDITOR'S NOTE—The Abstracts this month represent some notes taken on a few of the papers presented before the Scientific Section of the American Pharmaceutical Association at its Annual Meeting at Dallas, Texas, August 24-29, 1936.]

Sodium Formaldehydesulfoxylate as a Preservative. J. C. Krantz, Jr., R. Musser and C. J. Carr. Sodium formaldehydesulfoxylate, a substance possessing definite reducing properties, was studied from the standpoint of its capacity to prevent changes in color of certain solutions upon aging. Among the solutions studied were those of epinephrine, physostigmine, morphine sulfate and a combination of sodium bicarbonate and sodium salicylate. Concentrations of sodium formaldehydesulfoxylate of 1-500, 1-1000, and 1-5000 were all found to prevent discoloration of these solutions upon aging. The fact that the sodium salicylate-sodium bicarbonate solution remained colorless in the presence of this reducing agent indicated that in all probability the usual color change is an oxidation process.

The addition of the sodium formaldehydesulfoxylate did not alter the therapeutic action of the drugs studied with the exception of epinephrine, whose activity was destroyed.

The Stability of Digitalis as a Drug. L. W. Rowe and H. W. Pfeifle. The method of storage prescribed for digitalis in the Pharmacopœia was adopted on the basis of the rapid deterioration which has been reported for digitalis leaves when improperly stored. These authors report results of biological assays carried out on a series of samples of digitalis leaves which were stored under various conditions for six years. The variables were exposure or non-exposure to air, defatted or non-defatted leaves, storage at room temperature or refrigeration. In all cases the leaves were first dried in an oven between 60-70° C. The results obtained were of interest in that very little deterioration was found in any case. The presence of fat seemed to be the largest factor causing deterioration and even this did not cause a very considerable loss of activity.

The Pharmacognosy of the Anterior and Posterior Pituitary of Cattle. H. B. Youngken. The author reported a technique for distinguishing the powdered anterior and posterior lobes of pituitary. In the past these powdered drugs have been subject to adulteration and substitution because of the lack of an adequate method for determining their purity. The method developed depends upon the differential staining of definite microscopic elements using a combination of stains, namely, copperhematoxylin, eosin, and Weigert's differentiator. After staining, conspicuous chromophile cells with blue colored granules can be distinguished from pink stained chromophobe cells. The blue stained granular chromophile cells are characteristic and diagnostic of the anterior lobe. Small rounded blue stained basophile cells occurring in little patches are evident in the anterior lobe and the pars intermedia but rarely in the posterior lobe. The chief diagnostic elements of the posterior lobe were the stained pituicytes (modified astrocytes) which do not occur in the anterior lobe. A second differentiatiating factor is the segments of non-medullated nerve fibers with bulbous ends. The latter were found to be best detected with Delafield's hematoxylin and eosin stains and with hematoxylin and phosphotungstic acid.

Experiments With a New Suppository Base. J. C. Bird. The disadvantages of cacao butter were set forth, namely, its objectionable odor, greasiness, low melting point, and its immiscibility with mucous fluids. The latter point would seem to prevent the desirable diffusion of incorporated water soluble medicaments and interfere with any intimate contact with the mucosa. Oil soluble medicaments, on the other hand, might be expected to remain preferentially dissolved in the excipient and thus isolated by the fatty layer causing inefficient therapeutic action. An attempt to overcome these disadvantages has been made by utilizing hydrophilic substances having low melting points and self-emulsifying properties. A substance "monolene" (propylene glycol monostearate) seems to provide such a suppository material. It was described as smooth, unctuous and non-greasy, having an affinity for water with which it swelled to form an oil-in-water emulsion. Its melting point was described as higher than that of cacao butter and it also was found to set more quickly and possess better storage properties.

Pharmacological tests showed retention with total absence of irritation followed, usually, by soft, bulky, well-formed feces. The absence of remnants indicated complete emulsification with the excreta.

Animal and clinical tests involving various incorporated medicaments, per rectum, have shown excellent absorption and in many cases prolonged effect. Furthermore, the unguentous emulsified mass formed in the rectal area apparently localizes more effectually the action of such insoluble substances as are frequently employed in rectal and vaginal diseases.

New Iodine-Bile Compounds (Iodocholeates): Their Physical and Chemical Properties, Germicidal and Pharmacologic Action. P. Goedrich. The usual preparations of iodine such as the tincture and Lugol's solution are known to be irritating to animal tissue. The author with this in mind studied various iodine compounds. The combination of iodine with bile (iodocholeates) was of striking interest. In the first place bile salts possess a marked affinity for iodine even in the dry state. The compounds formed are probably of the adsorption type. They are dark brown and crystalline in appearance, soluble in water and alcohol without the addition of iodides. The solutions are stable and have the color of tincture of iodine. They are only slightly volatile and may be concentrated by evaporation in an open vessel on a water bath. The iodocholeates combine less readily with organic matter such as serum, mucous, etc., and are less corrosive to metal and rubber than tincture of iodine. Most remarkable of all is their germicidal activity which is practically two times that of iodine in the form of the tincture of the same strength. Applied to the unbroken skin the iodocholeates are practically non-irritating, even under heavy bandages, and they do not interfere with the healing processes as does the tincture and other caustic germicides. Animal and clinical results were reported illustrating very definitely these results.

Stabilized Syrup of Ferrous Iodide. P. L. Burrin, A. G. Worton and F. E. Bibbins. A study of syrup of ferrous iodide from the standpoint of maintaining it in stable form produced the following results:

1. A combination of dextrose and glycerin instead of sucrose provides a stable product.

2. If more than 30 per cent. glycerin is employed the product becomes slightly yellow.

3. The addition of 0.5 per cent. of sodium citrate or the replacement of the hypophosphorous acid by citric produces a stable product.

A Contribution to the Pharmacology of Pinacolone. J. C. Krantz, Jr., C. J. Carr, R. Musser and F. Beck. Pinacone is known to possess a marked hypnotic action. The authors prepared pinacolone which may be regarded as pinacone less one molecule of water and studied it for its pharmacological properties. Pinacolone is an oily liquid with a camphoraceous odor, sparingly soluble in water, but soluble in the ethereal solvents. It was found to be inert bactericidally, a mild depressant and local anesthetic action. When tested for its hypnotic action it was found to produce convulsions and respiratory failure. The conclusions of the authors were that pinacolone does not possess the hypnotic properties of pinacone.

A Note on the Magnesia Magma Heavy Metals Test. A. Osol and L. F. Tice. The U. S. P. XI test for heavy metals in magnesia magma is considered poorly worded in that the preparation of the standard lead solution for nephelometric comparison with the sample may or may not be acidified with hydrochloric acid depending upon the interpretation of the directions. This ambiguity is of particular significance inasmuch as the test is either very stringent or quite lenient, depending upon whether the acid is or is not added. It was found that if the standard were not acidified as much as 50 p. p. m. of lead could be present in a sample of magnesia magma and it would still pass the test, whereas if acidified very few of commercial magmas would pass the test. The interpretation according to the chairman of the U. S. P. Sub-Committee on Inorganic Chemicals was that the acid was not to be added to the standard.

This is subject to criticism as obviously both should receive identical treatment, otherwise the intent of the Pharmacopœia to set the limit Pb at 10 p. p. m. is meaningless. Experiments were performed with the purpose of adjusting both standard and sample at the same

pH, but the highest pH practical using a highly ionized acid like hydrochloric still prevented the development of a sufficient color to make comparison practical.

When acetic acid (5 cc. 36 per cent.), however, was employed both in the preparation of the sample and the standard lead solution the resulting pH values were 4.5 and 4.3 respectively, and the color developed by the H_2S was sufficiently pronounced to make comparison possible. The anomalous behavior of the standard when prepared with and without hydrochloric acid was explained by the authors as due to the variation in particle size of insoluble sulfides with change in hydrogen-ion concentration which is according to accepted theories due to the repression of ionization of hydrogen sulfide resulting in a diminution in hydrosulfide ions and a lowered stability on the part of the metallic sulfide particle. This is then reflected in a growth in particle size of the sulfide sol which according to Rayleigh's formula would result in lower light scattering power.

It is recommended by the authors that 5 cc. of 36 per cent. acetic acid replace the 5 cc. of hydrochloric acid prescribed by the official method, that it be added to both sample and standard and finally that the limit of lead permitted be raised to 20 p. p. m. in magnesia magma.

A Study of Solution of Magnesium Citrate. A. Osol and L. F. Tice. Experimental batches of Solution of Magnesium Citrate U. S. P. XI were prepared in which the MgO content, the addition of $KHCO_3$ and sterilization were the variable factors. Precipitation resulted in all samples containing bicarbonate within three weeks. To prepare even a fairly stable product an amount of magnesium carbonate corresponding to 15 gm. of a 39.2 per cent. MgO carbonate (the lower U. S. P. limit) must be used or the potassium bicarbonate may be withheld until just before the solution is to be dispensed.

Analyses of six commercial samples of solution of magnesium citrate made by different large scale producers gave results indicating that one was far below the U. S. P. XI standards for both MgO and citric acid, and that in every case all or part of the bicarbonate had been deleted from the formula. This was criticized as being both illegal and inimical to the full therapeutic intent of the product. It was pointed out that the Pharmacopœia permits carbonation by CO_2 under pressure as a process that may be used in addition to the inclusion of bicarbonate and not as an alternative process.